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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,140	07/31/2006	Do-Man Kim	44352-0010-00-US	1077

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

MAIL DATE	DELIVERY MODE
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12/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/588,140	Applicant(s) KIM ET AL.	
	Examiner Christian L. Fronda	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/06, 3/07, 9/07, 12/07</u> . | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> . |

Continuation of Attachment(s) 6). Other: NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES.

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DETAILED ACTION

1. Claims 1-10 as listed in claim set of the preliminary amendment filed 07/31/2006 are pending and under consideration in this Office Action.
2. The information disclosure statements (IDS) submitted on 07/31/2006, 03/26/2007, 09/17/2007, and 12/03/2007 have been considered and a signed copy of form PTO-1449 for each IDS is enclosed with the instant Office Action.
3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.
4. The specification is objected to for failing to supply a sequence identifier to all disclosed sequences. According to MPEP § 2422 sequences in the specification and claims must use a sequence identifier preceded by "SEQ ID NO". In particular, the nucleotide sequences on page 10, lines 6-14, and page 11, lines 27-28, lack sequence identifiers. Furthermore, the particular sequences are not present in the paper copy and computer readable copy of sequence listing. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821-1.825. Applicant must provide a substitute computer readable form (CFR) copy of the sequence listing, a substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same as required by 37 CFR 1.821-1.825.
5. Claims 1 and 2 are objected to for reciting the phrase "SEQ. ID. No.", which should be written as "SEQ ID NO". According to MPEP § 2422 sequences in the specification and claims must use a sequence identifier preceded by "SEQ ID NO".

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Claim Rejections - 35 U.S.C. § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1 and 2 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1 and 2 as written read on products of nature. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor (see MPEP 2105). For example, amending the claims to recite "A purified protein..." or "An isolated gene..." would obviate this rejection (see the specification, for example, page 8, lines 6-10; and page 10, line 25 to page 11, line 1).

Claim Rejections - 35 U.S.C. § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4 and 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein comprising the amino acid sequence of SEQ ID NO: 1 which has the activity of hydrolyzing dextran, starch, mutan, inulin, and levan; an isolated polynucleotide encoding said protein comprising the nucleotide sequence of SEQ ID NO: 2; a transformed prokaryotic or eukaryotic cell expressing said polynucleotide comprising

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the nucleotide sequence of SEQ ID NO: 2, a method for producing an enzyme having activity of hydrolyzing dextran, starch, mutan, inulin, and levan comprising culturing said transformed prokaryotic or eukaryotic cell expressing said polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2; and a composition comprising said enzyme produced by said method, wherein said composition is used for dextran removal during sugar production, for plaque elimination, or as a mouth wash; **does not** reasonably provide enablement for any derivative or any fragment of a protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity; any gene of SEQ ID NO: 2; and any derivative or any fragment of a gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

According to MPEP 2164.01(a), factors considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

MPEP § 2164.04 states that while the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. Accordingly, the factors most relevant to the instant rejection are addressed in detail below.

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The breadth of the claims: Claim 1 encompasses any derivative or any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity. In the absence of any specific definition for the term “derivative” from the instant specification, a “derivative” of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 is broadly interpreted to be any protein of any biological function comprising an altered amino acid sequence having one or more amino acid modifications in SEQ ID NO: 1, where such modifications include amino acid substitution, addition, deletion, and combinations thereof. A “fragment” of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 is broadly interpreted to be any protein of any biological function comprising any fragment of SEQ ID NO: 1.

Claim 2 encompasses any derivative or any fragment of the claimed gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity. In the absence of any specific definition for the term “derivative” from the instant specification, a “derivative” of the claimed gene of SEQ ID NO: 2 is broadly interpreted to be any polynucleotide of any biological function comprising an altered nucleotide sequence having one or more nucleotide modifications in SEQ ID NO: 2, where such modifications include nucleotide substitution, addition, deletion, and combinations thereof. A “fragment” of the claimed gene of SEQ ID NO: 2 is broadly interpreted to be any polynucleotide of any biological function comprising any fragment of SEQ ID NO: 2. Furthermore, gene elements which are not particularly described by the specification, including regulatory elements, introns, and untranslated regions, are essential to the function of the invention of claim 2 and are encompassed by claim 2 since the claim recites a “gene of SEQ ID NO: 2”.

The state of the prior art; The relative skill of those in the art; and The predictability or unpredictability of the art: It is well known in the prior art that the amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence to obtain a desired biological activity requires knowledge and guidance regarding specific amino acid residue(s) in the protein's amino

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acid sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification) and detailed knowledge of the protein's structure, and the ways in which the protein's structure relates to its function. The reference of Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teaches that the complexity of the structure/function relationship in enzymes has proven to be the factor limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships.

The positions within a protein's amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a protein having the same biological activity are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions, deletions, additions, and combinations thereof.

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene of SEQ ID NO: 2 with an expectation of obtaining a protein derivative and its encoding gene derivative having the same biological activity. At the time of the invention, there was a high level of unpredictability associated with altering a protein sequence with an expectation that the protein will maintain the same desired biological activity. For example, the reference of Witkowski et al. (Biochemistry. 1999 Sep 7; 38(36): 11643-50; PTO 892) teaches that only a single amino acid substitution results in conversion of the activity of a protein to a second, distinct activity (see e.g., Table 1, page 11647). In addition, the reference of Seffernick et al. (J Bacteriol. 2001 Apr; 183 (8): 2405-10; PTO 892) teaches that two proteins with 98% amino acid sequence identity were found to catalyze different reactions, where one protein has melamine deaminase activity and the other protein has atrazine chlorohydrolase activity (see Fig.3, page 2408; **DISCUSSION** section on

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page 2409).

Gene elements which are not particularly described by the specification, including regulatory elements, introns, and untranslated regions, are essential to the function of the invention of claim 2 since the claim recites a “gene of SEQ ID NO: 2”. Additionally, SEQ ID NO: 2 is disclosed as being essential to the function of the claimed invention since it encodes a protein comprising an amino acid sequence of SEQ ID NO: 1. The art indicates that the structure of genes which have regulatory elements, introns, and untranslated regions is empirically determined. For example, the structural elements of “gene” mediating the expression of a particular protein in the liver may be different than the structural elements of the “gene” mediating the expression of the same protein in the brain. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art. The reference of Attwood (Science. 2000 Oct 20; 290: 471-473); PTO 892) teaches uncertainty in predicting the number of genes and their introns and exons in an organism, such as *Drosophila* and human, and uncertainty in the definition of “gene” because it is unclear if a “gene” encodes a protein or proteins or is translated or untranslated.

The amount of direction provided by the inventor; and The existence of working examples: The specification discloses one working example, which is an isolated polynucleotide obtained from *Lipomyces starkeyi* KFCC-11077 encoding a protein having dextranase activity and comprising the amino acid sequence of SEQ ID NO: 1, where said protein has the activity of hydrolyzing dextran, starch, mutan, inulin, and levan. However, the specification fails to disclose any specific guidance for altering the protein comprising the amino acid sequence of SEQ ID NO: 1 and its encoding gene of SEQ ID NO: 2 with the expectation that the protein will maintain the same biological activity. In particular, the specification fails to disclose any specific guidance for altering the protein comprising the amino acid sequence of SEQ ID NO: 1 and its encoding gene of SEQ ID NO: 2 with the expectation that the protein will still have dextranase activity, because guidance and working examples teaching unalterable structural and catalytic amino acid residues and amino acid residues tolerable to change are not provided by the

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specification.

The specification does not provide specific guidance regarding any biological function or any specific and substantial use for the claimed derivative or fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1. The specification does not provide guidance regarding any specific biological function or any specific and substantial use for the claimed derivative or fragment of the claimed gene of SEQ ID NO: 2. Further, the term “A protein comprising an amino acid sequence of SEQ ID NO: 1” encompasses a full-length sequence as well as a fragment thereof because of “an”.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and the structure of the non-described regulatory elements, introns, and untranslated regions of the “gene of SEQ ID NO: 2”. The specification does not provide a specific guidance for regulatory elements, introns, and untranslated regions of the “gene of SEQ ID NO: 2”, let alone any fragment or derivative thereof. Therefore, the specification does not provide specific guidance for the claimed “gene of SEQ ID NO: 2”.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating and/or generating variants of a protein were known in the art at the time of the invention and the specification provides general teachings for searching and screening for the claimed invention, it was not routine in the art to screen by a trial and error process for all proteins having a substantial number of modifications as encompassed by the claim(s) for those that maintain the same desired biological activity. It was not routine in the art to screen and search for a specific any specific biological function or any specific and substantial use for the claimed derivative or fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1. It was not routine in the art to screen and search for a specific biological function or any specific and substantial use for the claimed derivative or fragment of the claimed gene of SEQ ID NO: 2. Screening for the claimed invention is not specific guidance on how to make the claimed invention.

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Therefore, in view of the overly broad scope of the claims, the specification's lack of specific guidance and additional working examples, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, it would require undue experimentation for a skilled artisan to make and use any derivative or any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity, and any derivative or any fragment of the claimed gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity

Such undue experimentation involves searching and screening a vast number of biological sources for any derivative of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene, and determine its biological function, where such derivative has an altered amino acid sequence having one or more amino acid modifications in SEQ ID NO: 1 (e.g., amino acid substitution, addition, deletion, and combinations thereof).

Undue experimentation involves searching and screening a vast number of biological sources for any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene with its regulatory elements, introns, and untranslated regions; and ascertaining its biological function.

Such undue experimentation also involves trial and error searching and screening for any one or more amino acids in SEQ ID NO: 1 to change (e.g., amino acid deletion, insertion, substitution, and combinations thereof) to thereby make a "derivative" of the claimed protein comprising the amino acid sequence of SEQ ID NO: 1, determining its biological function, and then searching for and/or synthesizing the polynucleotide encoding this protein "derivative".

Undue experimentation involves searching and screening a vast number for any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene with its regulatory elements, introns, and untranslated regions; and ascertaining its biological function.

General teachings from the specification regarding screening and searching for the claimed invention is not specific guidance for making and using the claimed invention.

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Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)).

Dependent claims 3, 4, and 6-10 are included in the rejection because these claims do not correct the defect of claims 1 or 2.

10. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the recited *Saccharomyces cerevisiae* deposited with accession number KCTC 10574BP recited in claim 5 is required to practice the claimed invention. As such the said *Saccharomyces cerevisiae* of accession number KCTC 10574BP must be readily available or obtainable by a repeatable method stated in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC § 112, first paragraph, may be satisfied by a deposit of the *Saccharomyces cerevisiae* of accession number KCTC 10573BP. See 37 CFR 1.801-1.809.

The process disclosed in the specification to make the said *Saccharomyces cerevisiae* of accession number KCTC 10574BP does not appear to be repeatable. The nucleotide sequence of the plasmid pYLSD1 is not fully disclosed, nor have all the nucleotide sequences required for its construction been shown to be biblically known and freely available. The specification does not disclose a repeatable process to obtain the said *Saccharomyces cerevisiae* of accession number KCTC 10574BP and it is not apparent if the nucleotide sequences to make the plasmid pYLSD1

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are readily available to the public. It is not apparent if the source materials to make the said *Saccharomyces cerevisiae* deposited with accession number KCTC 10574BP recited in claim are both known and readily available to the public.

Applicants' referral to deposit number KCTC 10574BP and its date of deposit in the specification on page 8, lines 1-3, is noted but is considered insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met since there is no indication in the specification as to its public availability.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the said *Saccharomyces cerevisiae* deposited with accession number KCTC 10574BP has been deposited under the Budapest Treaty and that the said *Saccharomyces cerevisiae* deposited with accession number KCTC 10574BP will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

11. Claims 1-4 and 6-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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According to MPEP 2163, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Claim 1 is drawn to any derivative or any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity. Claim 2 is drawn to any derivative or any fragment of the claimed gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity. The derivative or fragment recited in claims 1 and 2 do not recite any particular and specific structure to function relationship. The claims do not require that the derivatives or fragments possess any particular biological activity, any particular conserved structure, or any other distinguishing feature

Therefore, claim 1 is drawn to a genus of derivatives or fragments of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivatives or fragments have any amino acid sequence and any biological activity. Claim 2 is drawn to a genus of derivatives or fragments of the claimed gene of SEQ ID NO: 2, where the said derivatives or fragments have any nucleotide sequence and any biological activity.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties such as widely differing amino acid sequences, nucleotide sequences, and biological functions. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by

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functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

The instant specification discloses only one isolated protein comprising the amino acid sequence of SEQ ID NO: 1 and only one isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2 which encodes said isolated protein comprising the amino acid sequence of SEQ ID NO: 1. The instant specification discloses that the isolated protein comprising the amino acid sequence of SEQ ID NO: 1 has dextranase activity.

However, the instant specification does not describe and define any structural features, amino acid sequences, nucleotide sequences, and/or biological functions that are commonly possessed by members of each claimed genus. The specification does not describe any biological function for the claimed derivative or fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1. The specification does not describe any specific biological function for the claimed derivative or fragment of the claimed gene of SEQ ID NO: 2.

The specification fails to disclose a representative number of species of each claimed genus, which includes many members with widely differing structural, chemical, and biological functions. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the isolated protein comprising the amino acid sequence of SEQ ID NO: 1 is insufficient to be representative of the attributes and features common to all the members of the claimed genus of derivatives or fragments of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivatives or fragments have any amino acid sequence and any biological activity. Furthermore, the isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2 is insufficient to be representative of the attributes and features common to all the members of the claimed genus of

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derivatives or fragments of the claimed gene of SEQ ID NO: 2, where the said derivatives or fragments have any nucleotide sequence and any biological activity. Thus, one skilled in the art cannot visualize or recognize the identity of members of each claimed genus.

Furthermore, gene elements which are not particularly described by the specification, including regulatory elements, introns, and untranslated regions, are essential to the function of the invention of claim 2 since the claim recites a "gene of SEQ ID NO: 2". Additionally, SEQ ID NO: 2 is disclosed as being essential to the function of the claimed invention since it encodes a protein comprising an amino acid sequence of SEQ ID NO: 1. The art indicates that the structure of genes encompassing regulatory elements, introns, and untranslated regions is empirically determined. For example, the structural elements of "gene" mediating the expression of a particular protein in the liver may be different than the structural elements of the "gene" mediating the expression of the same protein in the brain. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and the structure of the non-described regulatory elements, introns, and untranslated regions of the "gene of SEQ ID NO: 2". The specification does not provide a complete detailed description of regulatory elements, introns, and untranslated regions of the "gene of SEQ ID NO: 2" let alone any fragment or derivative thereof. Therefore, the specification does not provide a written description of the claimed "gene of SEQ ID NO: 2".

Vas-Cath, Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d

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1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class, where the specification provided only the bovine sequence.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of derivatives or fragments of a protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivatives or fragments have any amino acid sequence and any biological activity; a genus of derivatives or fragments of a gene of SEQ ID NO: 2, where the said derivatives or fragments have any nucleotide sequence and any biological activity; and a "gene of SEQ ID NO: 2". Therefore, only an isolated protein comprising the amino acid sequence of SEQ ID NO: 1 and an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2 meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112, first paragraph, is severable from its enablement provision (see page 115).

Claims 3, 4, and 6-10 are included in the rejection because these claims do not correct the defect of claim 2.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (US Patent 6,485,953, published 11/26/2002; PTO 892).

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Kim et al. teach an isolated enzyme named DXAMase obtained from *Lipomyces starkeyi* KFCC-11077 (*L. starkeyi* KSM 22), which has dextranase activity and a molecular weight of 60 kilo Daltons on SDS-PAGE. Because the disclosed protein comprising an amino acid sequence of SEQ ID NO: 1 and the reference DXAMase are both obtained from the same source *Lipomyces starkeyi* KFCC-11077, have about the same molecular weight, have the same disclosed dextranase activity, and hydrolyze starch and levan; then in absence of facts to the contrary, the reference DXAMase inherently has the same amino acid sequence of SEQ ID NO: 1 and has the same dextranase activity as the claimed protein, such as hydrolyzing starch, mutan, inulin, and levan. See entire patent, especially claim 1; column 2, line 8 to column 3, line 18; column 4, lines 17-52; column 5, line 14 to column 10, line 12, in particular.

Claims 7-10 which are product-by-process claims are included in the rejection because according to MPEP § 2113:

“[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985) (citations omitted)”

Kim et al. teach a mouthwash composition comprising the reference DXAMase, which is used for plaque elimination. See entire patent, especially claim 1; column 2, lines 24-40; column 7, line 60 to column 10, line 12, in particular.

Kim et al. teach that the DXAMase having a molecular weight of 60 kilo Daltons is obtained from *Lipomyces starkeyi* KFCC-11077 (*L. starkeyi* KSM 22) using gel permeation chromatography, where an eluted fraction containing citrate phosphate buffer solution and the DXAMase having dextranase activity was collected. See column 4, lines 34-53.

Claim 9 is included in the rejection because a product is a product, irrespective of its intended use. A recitation of the intended use of the claimed invention must result in a structural

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difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Thus, the reference teachings of Kim et al. anticipate the claims.

14. Claims 1-4 and 6-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Campana et al. (US Patent 5,637,491, published 06/10/1997; PTO 892).

Because claim 1 recites "an amino acid sequence" of SEQ ID NO: 1, then the claim encompasses any protein comprising any fragment of SEQ ID NO: 1.

Campana et al. teach an isolated dextranase from the fungus *Penicillium minoluteum* comprising "an amino acid sequence" of SEQ ID NO: 1 of the instant application which is identified as SEQ ID NO: 2, wherein said dextranase comprises an amino acid sequence that is 78.3% identical to SEQ ID NO: 1. See below the alignment of the amino acid sequence of the reference dextranase comprising SEQ ID NO: 2 to SEQ ID NO: 1 of the instant application.

Alignment of SEQ ID NO: 2 of Campana et al. and SEQ ID NO: 1 of instant application

RESULT 1
US-08-354-618-2
; Sequence 2, Application US/08354618
; Patent No. 5637491
; GENERAL INFORMATION:
; APPLICANT: Campana, Hernan Roca
; APPLICANT: Garcia, Bianca Maria Garcia
; APPLICANT: Clark, Emilio Margollez
; APPLICANT: Curbelo, Dania Mateu
; APPLICANT: Boada, Julio Marcos Delgado
; APPLICANT: Martinez, Luis S. Herrera
; APPLICANT: Alvarez, Jos Alberto Cremata
; APPLICANT: Perez-Casta eda, Manuel Rafael Raices
; APPLICANT: Martinez, Maria Elena Gonz lez
; APPLICANT: Jim nez, Efrain Rodriguez
; TITLE OF INVENTION: Dextranase enzyme, method for its
; TITLE OF INVENTION: production and DNA encoding the enzyme
; NUMBER OF SEQUENCES: 5
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Ronald J. Baron
; ADDRESSEE: Hoffmann & Baron
; STREET: 350 Jericho Turnpike
; CITY: Jericho
; STATE: New York

Art Unit: 1652

; COUNTRY: United States of America
; ZIP: 11753
; COMPUTER READABLE FORM:
; MEDIUM TYPE: diskette - 3.5 inch, 1.44 Mb
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: Wordperfect 6.0 version B
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/354,618
; FILING DATE:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: CU 115/93
; FILING DATE: 14-December-1993
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 574 amino acids
; TYPE: amino acid
; STRANDEDNESS: unknown
; TOPOLOGY: unknown
; MOLECULE TYPE: protein
; HYPOTHETICAL: NO
; ORIGINAL SOURCE:
; STRAIN: Penicillium minioluteum HI-4
US-08-354-618-2

Query Match 78.3%; Score 2563.5; DB 1; Length 574;
Best Local Similarity 81.1%; Pred. No. 5.3e-228;
Matches 462; Conservative 49; Mismatches 58; Indels 1; Gaps 1;

Qy	40	NRTVCGSQLCTWWHDSGEINTGTPVQAGNVRQSRKYSVHVSLADRNQFYDSFVYESIPRN	99
Db	5	NNTHCGADFCTWWHDSGEINTQTPVQPGNVRQSHKYSVQVSLAGTNNFHDSSFVYESIPRN	64
Qy	100	GNGRIYSPTDPPNSNTLNSSIDDGISIEPSLGINMAWSQFEYRRDVDIKITTIDGSILDG	159
Db	65	GNGRIYAPTDPNSNTLDSSVDDGISIEPSIGLNMAWSQFEYSHDVDVKILATDGSSSLGS	124
Qy	160	PLDIVIRPTSVKYSVKRC-VGGIIIRVPYDPNGRKFSVELKSDLYSYLSDGSQYVTSGGS	218
Db	125	PSDVVIRPVSISYAISQSDGGIVIRVPADANGRKFSVEFKTDLYTFLSDGNEYVTSGGS	184
Qy	219	VVGVEPKNALVIFASPFLLPRDMVPHMTPHDTQTMKPGPINNGDWGSKPILYFPPGVYWMN	278
Db	185	VVGVEPTNALVIFASPFLLPSGMIPHMTDNTQTMTPGPINNGDWGAKSILYFPPGVYWMN	244
Qy	279	EDTSGNPGKLGSNHMRDLPNTYVWHLAPGAYVKGAIEYFTKQNFYATGHGVLSGENYVYQ	338
Db	245	QDQSGNSGKLGSNHIRLNSNTYVWVYLAPGAYVKGAIEYFTKQNFYATGHGILSGENYVYQ	304
Qy	339	ANAADNYAVKSDGTSLRMWWHNNLGGGQTWFCMGPTINAPPFNTMDFNGNSNISSRISD	398
Db	305	ANAGDNYIAVKSDSTSLRMWWHNNLGGGQTWYCVGPTINAPPFNTMDFNGNSGISSQISD	364
Qy	399	YKQVGAYFFQTDGPEIYEDSVVHDFVHVNDDAIKTYYSYGASISRATIWKCHNDPIIQMG	458
Db	365	YKQVGAFFFQTDGPEIYPNSVVHDFVHVNDDAIKIYYSGASVSRATIWKCHNDPIIQMG	424
Qy	459	WTSRNLTGISIDNLHVIHTRYFKSETVVPISAIIGASPFYASGMTVDPSESISMTISNVVC	518

Db	425	WTSRDISGVTIDTLNVIHTRYIKSETVVP	SAIIGASPFYASGMSPDRSRKSISMTVSNVVC	484
Qy	519	EGLCPSLFRITPLQSYNNLVVKNAVFPDGLQTNP	IGIGESIIPAASGCTMDLEITNWTVK	578
		: :		
Db	485	EGLCPSLFRITPLQNYKNFVVKNVAFPDGLQTN	SIGTGESIIPAASGLTMGLNISNWTVG	544
Qy	579	GQKVTMQNFGSGSLGQFDIDGSYGQWSIN	608	
		: : :		
Db	545	GQKVTMENFOANSLGOFNIDGSYGGEWOIS	574	

Campana et al. teach an isolated cDNA from the fungus *Penicillium minoluteum* comprising the nucleotide sequence of SEQ ID NO: 1 encoding the reference dextranase comprising the amino acid sequence of SEQ ID NO: 2, where said isolated cDNA comprising the nucleotide sequence of SEQ ID NO: 1 has 71.2% similarity to the claimed gene of SEQ ID NO: 2. See below the alignment of SEQ ID NO: 1 of Campana et al. to SEQ ID NO: 2 of the instant application.

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Alignment of SEQ ID NO: 1 of Campana et al. and SEQ ID NO: 2 of instant application

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RESULT 1
US-08-354-618-1
; Sequence 1, Application US/08354618
; Patent No. 5637491
; GENERAL INFORMATION:
; APPLICANT: Campana, Hernan Roca
; APPLICANT: Garcia, Bianca Maria Garcia
; APPLICANT: Clark, Emilio Margollez
; APPLICANT: Curbelo, Dania Mateu
; APPLICANT: Boada, Julio Marcos Delgado
; APPLICANT: Martinez, Luis S. Herrera
; APPLICANT: Alvarez, Jos Alberto Cremata
; APPLICANT: Perez-Casta eda, Manuel Rafael Raices
; APPLICANT: Martinez, Maria Elena Gonz lez
; APPLICANT: Jim nez, Efrain Rodriguez
; TITLE OF INVENTION: Dextranase enzyme, method for its
; TITLE OF INVENTION: production and DNA encoding the enzyme
; NUMBER OF SEQUENCES: 5
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Ronald J. Baron
; ADDRESSEE: Hoffmann & Baron
; STREET: 350 Jericho Turnpike
; CITY: Jericho
; STATE: New York
; COUNTRY: United States of America
; ZIP: 11753
; COMPUTER READABLE FORM:
; MEDIUM TYPE: diskette - 3.5 inch, 1.44 Mb
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: Wordperfect 6.0 version B
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/354,618
; FILING DATE:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: CU 115/93
; FILING DATE: 14-December-1993
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 3629 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; STRAIN: Penicillium minioluteum HI-4
US-08-354-618-1

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Query Match          44.5%; Score 914; DB 2; Length 3629;
Best Local Similarity 71.2%; Pred. No. 4.1e-287;
Matches 1221; Conservative 0; Mismatches 490; Indels 3; Gaps 1;

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Qy      159 AACAGAACTGTTTGC GGGAGTCAACTCTGCACATGGTGGCACGACTCCGGCGAGATAAAC 218
      || |. || ||||| | ||| || ||||| || || || ||||| ||
Db      1238 AATAATACCCATTGCGGCGCCGATTTCGTACCTGGTGGCATGATTCAGGGGAGATCAAT 1297

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Qy	219	ACGGGTACTCTCTGTACAGGCAGGAACGTTTCGACAATCCCGAAAGTACTCTGTCCATGTG	278
Db	1298	ACGCAGACACCTGTCCAACCAGGGAACGTGCGCCAATCTCACAAGTATTCGCTGCAAGTG	1357
Qy	279	AGCCTGGCAGACCGTAACCAATTCTACGACTCTTTTCGTATATGAATCGATACCTAGGAAC	338
Db	1358	AGCCTAGCTGGTACAAACAATTTTCATGACTCCTTTGTATATGAATCGATCCCCGGAAC	1417
Qy	339	GGCAATGGCAGAATTTATTCTCCCACCGACCCACCTAACAGCAATACATTGAATAGTAGC	398
Db	1418	GGAAATGGTCGCATCTATGCTCCCACCGATCCACCCAACAGCAACACACTAGATTCAAGT	1477
Qy	399	ATTGACGACGGTATATCAATCGAACCATCTCTCGGCATCAACATGGCTTGGTCCCAGTTC	458
Db	1478	GTGGATGATGGAATCTCGATTGAGCCTAGTATCGGCCTTAATATGGCATGGTCCCAATTC	1537
Qy	459	GAATATAGACGAGATGTCGACATTAAGATTACTACAATCGATGGCTCAATATTGGATGGC	518
Db	1538	GAGTACAGCCACGATGTAGATGTAAAGATCCTGGCCACTGATGGCTCATCGTTGGGCTCG	1597
Qy	519	CCTTTGGACATTGTTATTTCGGCCGACTTCTGTTAAGTACTCAGTCAAAGATGT---GTG	575
Db	1598	CCAAGTGATGTTGTTATTTCGCCCCGTCTCAATCTCCTATGCGATTCTCAGTCTGACGAT	1657
Qy	576	GGTGGTATCATTATTAGAGTCCCTTATGATCCCAATGGTCGAAAATTCTCTGTTGAGTTA	635
Db	1658	GGTGGGATTGTCATCCGGGTCCAGCCGATGCGAACGGCCGCAAATTTTCAGTTGAGTTC	1717
Qy	636	AAGAGTGACCTTTACAGTTACCTCTCCGACGGTTCGCAATATGTGACCTCTGGAGGGAGC	695
Db	1718	AAAACTGACCTGTACACATTCTCTCTGATGGCAACGAGTACGTCACATCGGGAGGCAGC	1777
Qy	696	GTGGTTGGTGTGGAGCCAAAAATGCCCTGGTGATCTTTGCCAGCCCTTCTTGCCACGG	755
Db	1778	GTCGTCGGCGTTGAGCCTACCAACGCACTTGTGATCTTCGCAAGTCCGTTTCTTCTTCT	1837
Qy	756	GATATGGTTCCTCATATGACACCACACGACACCCAGACAATGAAGCCGGGCCCAATCAAT	815
Db	1838	GGCATGATTCTCTCATATGACACCCGACAACACGACAGACCATGACGCCAGGTCCTATCAAT	1897
Qy	816	AATGGGGACTGGGGTCAAAGCCTATACTCTACTTCCCGCTGGCGTATACTGGATGAAC	875
Db	1898	AACGGCGACTGGGGCGCAAGTCAATTCTTTACTTCCCACCAGGTGTATACTGGATGAAC	1957
Qy	876	GAGGATACCTCTGGTAACCCCGGGAAGCTCGGCTCAAATCATATGCGGCTGGATCCCAAT	935
Db	1958	CAAGATCAATCGGGCAACTCGGGGAAGTTAGGATCTAATCATATACGTCTAAACTCGAAC	2017
Qy	936	ACCTACTGGGTCCATCTAGCCCCAGGAGCCTATGTGAAAGGAGCCATTGAGTATTTACG	995
Db	2018	ACTTACTGGGTCTACCTTGCCCCGGTGCGTACGTGAAGGGTGCTATAGAGTATTTTACC	2077
Qy	996	AAGCAAAATTTCTATGCAACGGGTCTATGGCGTTCTCTCAGGTGAGAACTATGTTTATCAG	1055
Db	2078	AAGCAGAACTTCTATGCAACTGGTCATGGTATCCTATCGGGTGAAACTATGTTTACCAA	2137
Qy	1056	GCCAATGCAGCTGATAACTACTATGCCGTCAAGAGTGATGGCACAAGCTTGAGAATGTGG	1115

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Db      2138  GCCAATGCCGGCGACAACCTACATTGCAGTCAAGAGCGATTCAACCAGCCTCCGGATGTGG 2197
Qy      1116  TGGCACAACAACCTTGGAGGCGGTCAAACATGGTTTTGCATGGGGCCCACCATTAATGCA 1175
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2198  TGGCACAATAACCTTGGGGGTGGTCAAACATGGTACTGCGTTGGCCCGACGATCAATGCG 2257
Qy      1176  CCGCCGTTTAAATACGATGGACTTCAACGAAACTCTAATATTTCCAGCCGGATTAGTGAC 1235
        || || || ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2258  CCACCATTCAATACTATGGATTTCAATGGAAATTCTGGCATCTCAAGTCAAATTAGCGAC 2317
Qy      1236  TATAAGCAGGTTGGCGCTTATTTTTTCCAAACAGACGGACCGGAGATCTACGAGGACAGT 1295
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2318  TATAAGCAGGTGGGAGCCTTCTTCTCCAGACGGATGGACCAGAAATATATCCCAATAGT 2377
Qy      1296  GTTGTCCATGACGTCTTCTGGCATGTTAATGATGATGCCATCAAGACATATTATTCCGGA 1355
        || || || ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2378  GTCGTGCACGACGTCTTCTGGCACGTCAATGATGATGCAATCAAATCTACTATTCCGGA 2437
Qy      1356  GCTTCAATTTACGAGCAACCATCTGGAAGTGTCACAATGACCCGATCATAAGATGGGC 1415
        || || || || || ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2438  GCATCTGTATCGCGGGCAACGATCTGGAAATGTCACAATGACCCAATCATCCAGATGGGA 2497
Qy      1416  TGGACGTCAAGAAATCTACCGGAATCAGCATTGATAACCTGCACGTATCCACACGAGA 1475
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2498  TGGACGTCTCGGGATATCAGTGGAGTGACAATCGACACATTAAATGTTATTACACCCGC 2557
Qy      1476  TATTTCAAATCTGAAACAGTGGTTCCTTCAGCAATCATTTGGAGCGTCTCCATTCTACGCA 1535
        || || ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2558  TACATCAAATCGGAGACGGTGGTGCCTTCGGCTATCATTGGGGCCTCTCCATTCTATGCA 2617
Qy      1536  AGTGGAAATGACTGTTGATCCCAGCGAGTCCATCAGCATGACCATCTCTAACGTGGTGTGT 1595
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2618  AGTGGGATGAGTCCTGATTCAAGAAAGTCCATATCCATGACGGTTTCAAACGTTGTTTGC 2677
Qy      1596  GAGGGTCTATGCCCCTCACTGTTCCGTATCACTCCGCTTCAGAGCTACAACAACCTTGTT 1655
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2678  GAGGGTCTTTGCCCCTCCCTATTTCCGCATCACACCCCTTCAGAACTACAAAAATTTTGT 2737
Qy      1656  GTCAAGAACGTGGCCTTTCCCGATGGACTGCAGACAAATCCAATCGGAATAGGAGAGAGC 1715
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2738  GTCAAAAATGTGGCTTTCCAGACGGGTACAGACGAATAGTATTGGCACAGGAGAAAGC 2797
Qy      1716  ATTATACCAGCAGCTTCCGGCTGTACAATGGACTTGGAAATCACAACTGGACCGTCAAA 1775
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2798  ATTATTCAGCCGCATCTGGTCTAACGATGGGACTGAATATCTCCAATGGACTGTTGGT 2857
Qy      1776  GGACAAAAAGTCACCATGCAAACTTTCAAGTCCGGGTCACTTGGCCAGTTTCGATATCGAT 1835
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      2858  GGACAAAAAGTGACTATGGAGAAGTTCAAGCCAATAGCCTGGGGCAGTTCAATATTGAC 2917
Qy      1836  GGTTCATACTGGGGTCAATGGTCCATAAACTAAA 1869
        || || ||||| ||||| ||||| ||||| |||||
Db      2918  GGCAGCTATTGGGGGGAGTGGCAGATTAGCTGAA 2951

```

The said isolated cDNA comprising the nucleotide sequence of SEQ ID NO: 1 is deemed to be a “derivative” of the claimed gene of SEQ ID NO: 2 since it has a high nucleotide sequence

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similarity to SEQ ID NO: 2 of the instant application, and encodes the reference dextranase which inherently has the same activity as the claimed protein, such as having dextranase activity and hydrolyzing starch, mutan, inulin, and levan.

Campana et al. teach transformed cells, such as transformed transformed *Pichia pastoris* cells (eukaryotic) expressing the said isolated cDNA comprising the nucleotide sequence of SEQ ID NO: 1 encoding the reference dextranase. Campana et al. teach a method for producing the reference dextranase, comprising: culturing the transformed *Pichia pastoris* cells, expressing the reference dextranase in the cultured *Pichia pastoris* cells, the cultured *Pichia pastoris* cells are subjected to mechanical lysis with glass beads, the reference dextranase purified from the fermentation culture supernatant by consecutive centrifugations, the supernatant dialyzed against ammonium acetate buffer and applied to anion exchange column, and the reference dextranase eluted from the column with a linear gradient of ammonium acetate. See entire patent, especially Sequence Listing showing SEQ ID NO: 1, column 2, line 32 to column 5, line 3; column 6, line 33 to column 12, line 21.

The reference enzyme above purified from the fermentation culture supernatant is in a composition comprising ammonium acetate (see column 11, lines 27-35). Claims 8-10 are also included in the rejection because a composition is a composition, irrespective of its intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Thus, the reference teachings of Campana et al. anticipate the claims.

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Claim Rejections - 35 U.S.C. § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US Patent 6,485,953, published 11/26/2002) in view of Standing (Curr Opin Struct Biol. 2003 Oct;13(5):595-601; PTO 892) and Sambrook et al. (Molecular cloning A Laboratory Mannual, 2nd edition, Cold Spring Harbor, N.Y. 1989, pages 8.46-8.52 and pages 11.2-11.19; PTO 892). For the purpose of this art rejection, claim 2 has been interpreted as an isolated polynucleotide of SEQ ID NO: 2 which encodes a protein comprising an amino acid sequence of SEQ ID NO: 1.

The reference teachings of Kim et al. have been stated above. The teachings of Kim et al. differ from the claim in that Kim et al. does not teach an isolated polynucleotide of SEQ ID NO: 2 which encodes a protein comprising an amino acid sequence of SEQ ID NO: 1.

Standing teaches mass spectrometry methods to obtain the amino acid sequence of

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peptides and proteins, where *de novo* protein sequencing by mass spectrometry methods dates back more than 30 years (see entire publication, especially page 595, right column, second full paragraph to page 598, right column, last full paragraph).

Sambrook et al. teach widely known conventional methods to obtain and isolate the nucleic acid encoding a desired protein using the amino acid sequence of the desired protein to synthesize degenerate pools of oligonucleotide probes which are used to screen DNA libraries for the sought nucleic acid encoding the desired protein and recombinant protein expression and purification methods to obtain large amounts of recombinant proteins using expression vectors. See all volumes of Sambrook et al., especially pages 8.46-8.52 and pages 11.2-11.19.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the mass spectrometry methods taught by Standing to obtain the amino acid sequence of the DXAMase taught by Kim et al., and then use the obtained amino acid sequence of the DXAMase with the conventional methodologies taught by Sambrook et al. to thereby isolate the polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do the above because Kim et al. teach the DXAMase is useful for plaque elimination and for the purpose of obtaining the isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al., which can be then cloned into expression vectors and used in recombinant protein expression and purification methods to easily obtain large amounts of purified DXAMase as taught by Sambrook et al..

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success because of the high level of skill in the art since *de novo* protein sequencing by mass spectrometry methods dates back more than 30 years as taught by Standing, and molecular biology techniques for making synthetic oligonucleotide probes and DNA library screening are widely known and available. For example, see all volumes of

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Sambrook et al. (Molecular cloning A Laboratory Mannual, 2nd edition, Cold Spring Harbor, N.Y. 1989), which is a comprehensive collection of well-known molecular biology techniques.

This rejection is based on the decision of *Ex parte* MAREK Z. KUBIN and RAYMOND G. GOODWIN (*Ex Parte Kubin & Goodwin*, No. 2007-0819, 2007 WL 2070495 (Bd.Pat.App. & Interf. May 31, 2007), where the board relied heavily on *KSR* (*KSR Int'l Co. v. Teleflex Inc.*, 550 U.S.-, 82 USPQ2d 1385, 1394, 1396 (2007).

In *Ex parte* MAREK Z. KUBIN and RAYMOND G. GOODWIN, the board found that the claimed nucleic acid encoding the NAIL protein to be obvious over a reference that discloses the NAIL protein and a reference teaching methodologies for isolating the corresponding encoding cDNA. Relying on *KSR*, the board found that:

“Appellants heavily rely on *Deuel*. (See, e.g., Br. 19.) To the extent *Deuel* is considered relevant to this case, we note the Supreme Court recently cast doubt on the viability of *Deuel* to the extent the Federal Circuit rejected an “obvious to try” test. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, ___, 82 USPQ2d 1385, 1394, 1396 (2007) (citing *Deuel*, 51 F.3d at 1559). Under *KSR*, it’s now apparent “obvious to try” may be an appropriate test in more situations than we previously contemplated.

When there is motivation

to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007). This reasoning is applicable here. The “problem” facing those in the art was to isolate NAIL cDNA, and there were a limited number of methodologies available to do so. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. Thus, isolating NAIL cDNA was “the product not of innovation but of ordinary skill and common sense,” leading us to conclude NAIL cDNA is not patentable as it would have been obvious to isolate it.” (see pages 8-9).

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Accordingly, isolating the polynucleotide of SEQ ID NO: 2 encoding a protein comprising an amino acid sequence of SEQ ID NO: 1 is concluded to be the product not of innovation but of ordinary skill and common sense, and therefore, the polynucleotide of SEQ ID NO: 2 is not patentable as it would have been obvious to isolate.

17. Claims 3, 4, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US Patent 6,485,953, published 11/26/2002) in view of Standing (Curr Opin Struct Biol. 2003 Oct;13(5):595-601; PTO 892) and Sambrook et al. (Molecular cloning A Laboratory Manual, 2nd edition, Cold Spring Harbor, N.Y. 1989, pages 8.46-8.52 and pages 11.2-11.19; PTO 892) as applied to claim 2 above; and further in view of Guan et al. (US Patent 5,643,758, published 07/01/1997; PTO 892).

Guan et al. teach expression vectors containing nucleic acids encoding proteins such as beta-galactosidase fused to the *E.coli* maltose binding protein (MBP); isolated prokaryotic and eukaryotic host cells such as *E.coli* and yeast, respectively, transformed with said expression vectors; culturing methods for making and expressing any protein fused to said *E.coli* MBP by culturing said host cells under conditions suitable for the protein's expression (such as culturing in rich media) and recovering the produced protein in large, highly-purified quantities from the host cell culture by centrifugation, sonication, and chromatography including affinity chromatography targeting the *E.coli* MBP; and Guan et al. teach that that these methods and products are useful for purifying any protein (see entire publication of US Patent 5,643,758, especially column 1, lines 11-25; column 4, line 49 to column 9, line 49; and Examples I-IV found on column 9, line 66 to column 20, line 40). Guan et al. teach the successful expression, isolation, and purification of beta-galactosidase (see EXAMPLE I), PstI restriction endonuclease (see EXAMPLE II), and paramyosin (see EXAMPLE IV).

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Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the obtained isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al. into the expression vector of Guan et al. and the modified expression vector transformed into prokaryotic or eukaryotic host cells such as the *E. coli* and yeast cells, respectively, of Guan et al. to thereby make a transformed prokaryotic or eukaryotic cell expressing the obtained isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al. fused to the *E. coli* MBP. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the culturing method of Guan et al. such that the transformed prokaryotic or eukaryotic cell expressing the obtained isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al. fused to the *E. coli* MBP is cultured under conditions suitable for the expression of the DXAMase of Kim et al. and recovering the produced protein in large, highly-purified quantities from the host cell culture by centrifugation, sonication, and chromatography including affinity chromatography targeting the *E. coli* MBP.

One of ordinary skill in the art at the time the invention was made would have been motivated to do the above for the purpose of obtaining large, highly-purified quantities of the DXAMase of Kim et al. from the host cell. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success because Kim et al. teach DXAMase is useful for plaque removal, and Guan et al. teach that that these methods and products are useful for purifying any protein in large, purified quantities, and Guan et al. was successful in the expression, isolation, and purification of beta-galactosidase, PstI restriction endonuclease, and paramyosin.

Conclusion

18. No claim is allowed.

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19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM - 6:30PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian L. Fronda/

Patent Examiner

Art Unit 1652

Notice to Comply	Application No. 10/588,140	Applicant(s) KIM ET AL.	
	Examiner Christian L. Fronda	Art Unit 1652	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: The nucleotide sequences on page 10, lines 6-14, and page 11, lines 27-28, are not associated with a sequence identifier "SEQ ID NO" and is not included in the Sequence Listing. Furthermore, the sequences recited in claims 1 and 2 is not associated with a sequence identifier "SEQ ID NO".

Applicant Must Provide:

An substitute computer readable form (CRF) copy of the "Sequence Listing".

- ☒ An substitute paper copy of the "Sequence Listing", as well as an amendment specifically directing its entry into the application.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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